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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/373,828	08/13/99	FINCK B	2945

EXAMINER	
ROMEO, D	
ART UNIT	**PAPER NUMBER**
1647	12

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HM22/0316

DATE MAILED: 03/16/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.	Applicant(s)
09/373,828	Finck
Examiner	**Group Art Unit**
David Romeo	1647

☒ Responsive to communication(s) filed on *11 Jan 2001*.

☐ This action is **FINAL**.

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire *3* month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) *1-23* is/are pending in the application.

Of the above, claim(s) *8, 9, and 14-22* is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) *1-7, 10-13, and 23* is/are rejected.

☐ Claim(s) _____ is/are objected to.

☒ Claims *1-23* are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐approved ☐disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____.

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____.

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☒ Notice of References Cited, PTO-892

☒ Information Disclosure Statement(s), PTO-1449, Paper No(s). *5, 11*

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

DETAILED ACTION

1. The preliminary amendment filed 01/11/2001 (Paper No. 9) has been entered. Claims 1-23 are pending.

2. Applicant's election of group I, claims 1-13, in Paper No. 9 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

3. Claims 14-22 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in Paper No. 9.

4. It would appear from limitations "5" and "6" in claim 2, that claim 2 encompasses the treatment of psoriasis. The treatment of psoriasis and the treatment of psoriatic arthritis are independent and distinct for the reasons in the last Office action mailed 12/13/2000 (Paper No. 8). Accordingly, claim 2 is withdrawn from consideration to the extent that it is drawn to a method of treating psoriasis.

5. Applicant's election with traverse of the species celecoxib in Paper No. 9 is acknowledged. The traversal is on the ground(s) that it would not be an undue burden to examine to examine all the species. This is not found persuasive because Applicant is required under 35 U.S.C. 121 to elect a single disclosed species for prosecution on the merits to which the claims shall be restricted if no generic claim is finally held to be allowable. Upon the allowance of a generic claim, applicant will be entitled to consideration of claims to additional species which are written in dependent form or otherwise include all the limitations of an allowed generic claim as provided by 37 CFR 1.141.

The requirement is still deemed proper and is therefore made FINAL.

6. Claims 7-10 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), to the extent that they are drawn to a nonelected species, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in Paper No. 9.

7. Claims 1-7, 10-13, 23 are being examined to the extent that they read upon the elected invention and/or species.

8. The disclosure is objected to because of the following informalities: The specification at page 1, lines 5-8, contains blank spaces where U.S. patent application serial numbers are supposed to be.

Appropriate correction is required.

Claim Rejections - 35 USC § 112

9. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

10. The following claims are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

a. Claim 2 is indefinite over the recitation of "patient self-assessment" and "physician assessment" because it is unclear what is being "assessed" such that an improvement over baseline could be determined. The metes and bounds of the claim(s) are not clearly set forth.

b. Claim 1 is indefinite because it lacks a process step which clearly relates back to the claim preamble and it is unclear what process is to be achieved; an intended use is not the same as achieving a result; in the absence of a recitation as to any result, or a process step producing a result, it is unclear what result of the process can be inferred. For example, it is

unclear if the treatment of psoriatic arthritis or psoriasis is achieved, as indicated by the Markush group of claim 2. The metes and bounds of the claim(s) are not clearly set forth.

c. Claim 2 is indefinite because it contains a process step (limitations "5" or "6" in claim 2, which encompass the treatment of psoriasis) which does not clearly relate back to the claim preamble and it is unclear what process is to be achieved; it is unclear if the treatment of psoriatic arthritis or psoriasis is achieved. The metes and bounds of the claim(s) are not clearly set forth.

Claim Rejections - 35 USC § 103

11. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

12. Claims 1-7 are rejected under 35 U.S.C. 103(a) as being unpatentable over Moreland (u12)[1] and Partsch (cited by Applicants).

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[1]Citations by the examiner are in an alphanumeric format, such as "(a1)", wherein the "a" refers to the reference cited on the Notice of References Cited, PTO-892, and the "1" refers to the Paper No. to which the Notice of References Cited, PTO-892, is attached.

Moreland (u12) teaches that tumor necrosis factor (TNF) is a proinflammatory cytokine involved in the pathogenesis of rheumatoid arthritis, and antagonism of TNF may reduce the activity of the disease. Moreland evaluated the safety and efficacy of a novel TNF antagonist -- a recombinant fusion protein that consists of the soluble TNF receptor (p75) linked to the Fc portion of human IgG1 (TNFR:Fc). Treatment with TNFR:Fc led to significant reductions in disease activity, and the therapeutic effects of TNFR:Fc were dose-related. See page 141, column 1, Background and Results. Moreland teaches the administration by injection twice weekly for a period of three months of 0.25, 2, and 16 mg TNFR:Fc per square meter (page 142, column 2, Treatment). Moreland does not teach the treatment of PsA with TNFR:Fc.

Partsch (cited by Applicants) teaches that the pattern of expression of proinflammatory cytokines seen in psoriatic arthritis (PsA) is similar to that seen in rheumatoid arthritis (RA). Since PsA is also a destructive arthropathy, cytokines, in particular TNFα and IL1, may be principle factors in joint destruction (page 518, Conclusion). Clearly, TNFα, IL1, IL6, and IL8 are increased in synovial fluid (SF) of patients with PsA, a "destructive" inflammatory arthropathy; TNFα has a central position in the cascade of proinflammatory cytokines (page 521, column 1, full paragraph 2). TNFα is highly increased in the SF of patients with PsA compared to osteoarthritis (OA), indicating an important role of TNFα in PsA (page 521, paragraph bridging columns 1-2). Therapy directed to control of TNFα, which has been successful in RA, may also

be beneficial in PsA (page 522, column 1, full paragraph 2). Partsch does not teach the treatment of PsA with TNFR:Fc.

However, it would have been obvious to one of ordinary skill in the art at the time of Applicants' invention to control TNFα in RA with TNFR:Fc, as taught by Moreland, and to modify that teaching by controlling TNFα in PsA, as suggested by Partsch, with TNFR:Fc with a reasonable expectation of success. One of ordinary skill in the art would be motivated to combine these teachings because the pattern of expression of proinflammatory cytokines seen in PsA is similar to that seen in RA, PsA is also a destructive arthropathy, TNFα is increased in SF of patients with PsA, TNFα has a central position in the cascade of proinflammatory cytokines, TNFα is highly increased in the SF of patients with PsA indicating an important role of TNFα in PsA, and therapy directed to control of TNFα, which has been successful in RA, may also be beneficial in PsA. The invention is prima facie obvious over the prior art.

13. Claims 1, 7, 10, 23 are rejected under 35 U.S.C. 103(a) as being unpatentable over Moreland (u12) and Partsch (cited by Applicants) as applied to claims 1, 7 above, and further in view of Wallach (a12), Lipsky (v12), Gladman (cited by Applicants), and Salvarani (cited by Applicants).

Moreland and Partsch teach the treatment of PsA with TNFR:Fc. Moreland and Partsch do not teach the treatment of PsA with TNFR:Fc and celecoxib.

Wallach teaches compositions for treatment of rheumatoid arthritis comprising a sTNFR and other anti-inflammatory agents (column 7, lines 56-57).

Lipsky teaches that in patients with RA specific inhibition of COX-2 with celecoxib is sufficient to suppress the signs and symptoms of inflammatory disease activity (page 9, column 2, full paragraph 1; page 13). NSAID effectively prevents the development of inflammation in arthritis (page 10, column 2, full paragraph 1).

Gladman (cited by Applicants) teaches that treatment of inflammation is clearly indicated for the treatment of PsA (page 841, full paragraph 1).

Salvarani (cited by Applicants) teaches combination therapy for the treatment of PsA (paragraph bridging pages 302-303; page 303, column 1, last full paragraph).

Wallach, Lipsky, Gladman, and Salvarani do not teach the treatment of PsA with TNFR:Fc and celecoxib.

However, it would have been obvious to one of ordinary skill in the art at the time of Applicants' invention to treat PsA with TNFR:Fc, as taught by Moreland and Partsch, and to modify that teaching by administering other anti-inflammatory agents, as taught by Wallach, such as celecoxib, as taught by Lipsky, with a reasonable expectation of success. One of ordinary skill in the art would be motivated to combine these teachings because PsA is a "destructive" inflammatory arthropathy and combined anti-inflammatory therapy is efficacious for the treatment of inflammatory conditions, such as PsA. The invention is prima facie obvious over the prior art.

14. Claims 1, 11 are rejected under 35 U.S.C. 103(a) as being unpatentable over Moreland (u12) and Partsch (cited by Applicants) as applied to claim 1 above, and further in view of Jacobs (b12) and Wallach (a12).

Moreland and Partsch teach the treatment of PsA with TNFR:Fc. Moreland and Partsch do not teach administration of the TNFR:Fc in a sustained release form.

Jacobs teaches that for therapeutic use, purified soluble TNFR protein is administered to a patient, preferably a human, for treatment of arthritis. Thus, for example, soluble TNFR protein compositions can be administered, for example, via intra-articular, intraperitoneal or subcutaneous routes by bolus injection, continuous infusion, sustained release from implants, or other suitable techniques (column 13, lines 28-35).

Wallach teaches that controlled release systems deliver a drug at a predetermined rate for a definite time period, that may range from days to years. These systems provide advantages over conventional drug therapies. See column 1, lines 19-36. Wallach teaches approaches for therapeutic applications of soluble forms of receptors for affecting the functions of their ligands, e.g., for protection against deleterious effects of their ligands, particularly systems which allow local release of the soluble receptor in the body, at a constant rate and for long duration. These approaches are based on incorporation of the soluble receptor into biocompatible polymeric materials, which are implanted or injected in desired bodily compartments. Matrices of polymers containing the soluble receptor enable local and controlled release of the soluble receptor, in its

natural form. Any soluble receptor that is capable of binding to and affecting the functions of its ligand, either neutralizing the deleterious effects of its ligand and/or stabilizing or augmenting its activity, is encompassed by the invention. Examples of such soluble receptors are the soluble receptors of hormones and of cytokines, and in a preferred embodiment, the soluble receptor is a soluble TNFα receptor. See column 3, line 55, through column 4, line 8, and column 4, lines 38-45. Wallach teaches that the pharmaceutical composition of the invention comprising a sTNF-R may be used to neutralize the deleterious effects of TNFα in autoimmune diseases such as rheumatoid arthritis (column 7, lines 38-47). Wallach teaches that the compositions for treatment of rheumatoid arthritis may comprise other anti-inflammatory agents (column 7, lines 56-57).

Jacobs and Wallach do not teach administration of TNFR:Fc in a sustained release form encapsulated or admixed with a biocompatible polymer.

However, it would have been obvious to one of ordinary skill in the art at the time of Applicants' invention to treat PsA with TNFR:Fc, as taught by Moreland and Partsch, and to modify that teaching by administering the TNFR:Fc in a sustained release form, as taught by Jacobs, encapsulated or admixed with a biocompatible polymer, as taught by Wallach, with a reasonable expectation of success. One of ordinary skill in the art would be motivated to combine these teachings because controlled release systems provide advantages over conventional drug therapies. The invention is prima facie obvious over the prior art.

15. Claims 1, 12, 13 are rejected under 35 U.S.C. 103(a) as being unpatentable over Moreland (u12) and Partsch (cited by Applicants) as applied to claim 1 above, and further in view of Jacobs (b12).

Moreland and Partsch teach the treatment of PsA with TNFR:Fc, as discussed above and incorporated herein by reference. Moreland and Partsch are silent with the particulars of the administrations recited in claims 12 and 13. However, it would have been obvious to one of ordinary skill in the art at the time of Applicants' invention to treat any and all patients with PsA, such as those between the ages of 4 and 17, with a reasonable expectation of success and absent evidence to the contrary. It would have been further obvious to one of ordinary skill in the art at the time of Applicants' invention to vary the amount and frequency of administration depending, of course, on such factors as the nature and severity of the indication being treated, the desired response, the condition of the patient, and so forth, such that it would have been obvious to one of ordinary skill in the art at the time of Applicants' invention to administer TNFR:Fc in a dose of 0.3 mg/kg, up to a maximum of 25 mg, two or three times per week for one week or longer with a reasonable expectation of success and absent evidence to the contrary. For instance, Jacobs teaches that for therapeutic use, purified soluble TNFR protein is administered to a patient, preferably a human, for treatment of arthritis. Thus, for example, soluble TNFR protein compositions can be administered, for example, via intra-articular, intraperitoneal or subcutaneous routes by bolus injection, continuous infusion, sustained release from implants, or other suitable

techniques (column 13, lines 28-35). For treatment of arthritis, TNFR is administered in systemic amounts ranging from about 0.1 mg/kg/week to about 100 mg/kg/week. In preferred embodiments of the present invention, TNFR is administered in amounts ranging from about 0.5 mg/kg/week to about 50 mg/kg/week. For local intra-articular administration, dosages preferably range from about 0.01 mg/kg to about 1.0 mg/kg per injection. See column 14, lines 3-9. The amount and frequency of administration will depend, of course, on such factors as the nature and severity of the indication being treated, the desired response, the condition of the patient, and so forth (column 13, lines 52-55). The invention is prima facie obvious over the prior art.

Conclusion

16. No claims are allowable.

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DAVID ROMEO
PRIMARY EXAMINER
ART UNIT 1647

MARCH 16, 2001